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EXAMINER	
FORMAN, BETTY J	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/622,635	Applicant(s) KALLIONIEMI ET AL.	
	Examiner BJ Forman	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22,24-77 and 86-94* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22,27-77 and 86-94* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 5/01; 4/02; 10/02; 11/00
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. 304.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Prosecution on the merits of this application is reopened on claims 1-22, 24-77, 86-94 considered unpatentable for the reasons indicated below.

The amendment filed 16 April 2003 in which Claim 53 was amended has been entered.

The examiner for this application has changed. Please address future correspondence to Examiner BJ Forman, Art Unit: 1634.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 13, 22, 32-42, 58, 64, 65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 13 is indefinite for the recitation "biological sample" because the recitation lacks proper antecedent basis in Claim 1.

b. Claim 22 is indefinite for the recitation "less than about". The phrase "less than" typically indicates a maximum point. The phrase "less than" however, is contraverted by the term "about" which implies that values above and below 1mm are permitted. Further, the extent of variance permitted by "about" is unclear in this context because it is unclear if "about 1" simply includes 1.1 or if it also includes 1.5-2.0 as well. In Amgen, Inc. v. Chugai

Pharmaceutical Co., 927 F.2d 1200 (CAFC 1991), the CAFC stated, "The district court held claims 4 and 6 of the patent invalid because their specific activity limitation of "at least about 160,000" was indefinite". After review, the CAFC states "We therefore affirm the district court's determination on this issue." Thus, the CAFC found the phrase "at least about" indefinite where the metes and bounds of the term were not defined in the specification.

c. Claims 32-42 are indefinite in Claim 32, line 8 for the recitation "the result of screening multiple tissue specimens" because the recitation lacks proper antecedent basis in the "biological specimens" of line 5.

d. Claim 58 is indefinite for the recitation "an other characteristic" because the recitation lacks proper antecedent basis in Clam 53.

e. Claims 64 and 65 are each indefinite in that they are drawn to the array of claims 53 and 54 respectively. Claims 53 and 54 are drawn to a method of analyzing cellular specimens using an array. However, the method claims do not clearly define or describe the structural elements of the arrays. Therefore, one of ordinary skill in the art would not be appraised of the meets and bounds of Claims 64 and 65.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1, 2, 4, 6, 7, 13, 15 and 88 are rejected under 35 U.S.C. 102(b) as being anticipated by Lampkin et al (Journal of Histotechnology, 1990, 13(2): 121-123.

Regarding Claim 1, Lampkin et al disclose a method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (base mold), obtaining a plurality of copies of the recipient array such that the copies maintain their assigned locations, performing analysis of each copy and comparing the results of the analysis e.g. identification (page 122, left column, first and second full paragraphs and right column second full paragraph).

Regarding Claim 2, Lampkin et al disclose the method wherein the donor specimen is obtaining by boring (i.e. punched) an elongated sample from the specimen (paragraph bridging pages 121-122).

Regarding Claim 4, Lampkin et al disclose the method wherein the donor specimen is from a population of cells i.e. tissue (paragraph bridging pages 121-122).

Regarding Claim 6, Lampkin et al disclose the method wherein placing the donor specimen in an assigned location comprises forming an elongated receptacle in a donor block (Fig. 1D), obtaining an elongated specimen and obtaining a plurality of copies by sectioning the array transverse to the donor specimen (page 122, left column, first and second full paragraphs and Fig. 1).

Regarding Claim 7, Lampkin et al disclose the method wherein the donor specimen is placed in a receptacle having a size and shape "complementary" to the size and shape of the specimen (page 122, left column, first and second full paragraphs and Fig. 1). Lampkin teaches the donor specimens are placed into a grid-like base mold. Because the specimens

are placed in grid-like mold, the grid is deemed to have size and shape "complementary" to the specimens.

Regarding Claim 13, Lampkin et al disclose the method wherein the sample is a tissue specimen (paragraph bridging pages 121-122).

Regarding Claim 15, Lampkin et al disclose the method wherein placing the specimen comprises placing a sample in a "corresponding" position of the multiple copies i.e. the samples are aligned relative to the sectioned arrays (page 122, left column, first and second full paragraphs and Fig. 1).

Regarding Claim 88, Lampkin et al disclose a method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (base mold), obtaining a plurality of copies of the recipient array such that the copies maintain their assigned locations, performing analysis of each copy and comparing the results of the analysis e.g. identification (page 122, left column, first and second full paragraphs and right column second full paragraph).

6. Claims 1-7, 9-15, 49 and 88 are rejected under 35 U.S.C. 102(b) as being anticipated by Kraaz et al (Journal of Clinical Pathology, 1988, 41: 1337).

Regarding Claim 1, Kraaz et al disclose a method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (warm cast), obtaining a plurality of copies of the recipient array such that the copies maintain their assigned locations, performing analysis of each copy and comparing the results of the analysis i.e. immunostained and analyzed (center column and Fig. 1).

Regarding Claim 2, Kraaz et al disclose the method wherein the donor specimen is obtaining by boring (i.e. punched) an elongated sample from the specimen (center column, lines 1-7).

Regarding Claim 3, Kraaz et al disclose the method wherein the specimen is from a tumor (center column).

Regarding Claim 4, Kraaz et al disclose the method wherein the donor specimen is from a population of cells i.e. tissue (center column, lines 1-7).

Regarding Claim 5, Kraaz et al disclose the method wherein the donor specimen is from a cytological preparation i.e. tissue (center column, lines 1-7).

Regarding Claim 6, Kraaz et al disclose the method wherein placing the donor specimen in an assigned location comprises forming an elongated receptacle in a donor block (i.e. cast), obtaining an elongated specimen and obtaining a plurality of copies by sectioning the array transverse to the donor specimen (center column and Fig. 1).

Regarding Claim 7, Kraaz et al disclose the method wherein the donor specimen is placed in a receptacle having a size and shape "complementary" to the size and shape of the specimen (center column and Fig. 1). Kraaz teaches the donor specimen is placed into a cast. Because the specimens are placed in cast, the grid is deemed to have a size and shape "complementary" to the specimens.

Regarding Claim 9, Kraaz et al disclose the method further comprising associating a clinical characteristic with each assigned location i.e. each tumor specimen is assigned a position (center column, lines 1-7).

Regarding Claim 10, Kraaz et al disclose the method wherein a different analysis is performed on each array (center column, last paragraph).

Regarding Claim 11, Kraaz et al disclose the method wherein the analysis is immunological analysis (center column and Fig.. 1).

Regarding Claim 12, Kraaz et al disclose the method further comprising determining whether there are "correlations" between clinical characteristic "associated" with each location i.e. the tumor specimens are compared to controls (center column, second full paragraph).

Regarding Claim 13, Kraaz et al disclose the method wherein the sample is a tissue specimen (center column, lines 1-7).

Regarding Claim 14, Kraaz et al disclose the method wherein clinical characteristics are determined apart from array analysis and the characteristics are tumor grade, size or status i.e. various degrees of reactivity (center column, second full paragraph).

Regarding Claim 15, Kraaz et al disclose the method wherein placing the specimen comprises placing a sample in a "corresponding" position of the multiple copies i.e. the samples are aligned relative to the sectioned arrays (center column, lines 1-7).

Regarding Claim 49, Kraaz et al disclose the method wherein donor specimens are from one or more tumors (center column).

Regarding Claim 88, Kraaz et al disclose a method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (warm cast), obtaining a plurality of copies of the recipient array such that the copies maintain their assigned locations, performing analysis of each copy and comparing the results of the analysis i.e. immunostained and analyzed (center column and Fig. 1).

7. Claims 1-20, 22, 29-30, 43-44, 49, 53-61, 64-65, 70 and 87-92 are rejected under 35 U.S.C. 102(b) as being anticipated by Enghardt et al (Journal of Histotechnology, 1995, 18(1): 51-55).

Regarding Claim 1, Enghardt et al disclose a method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (cassette, and page 55, second full paragraph), obtaining a plurality of copies of the recipient array such that the copies maintain their assigned locations (page 53, right column "slides"), performing analysis of each copy and comparing the results of the analysis i.e. immunostained and analyzed (page 53, last paragraph-page 54, left column).

Regarding Claim 2, Enghardt et al disclose the method wherein the donor specimen is obtaining by boring (i.e. punched) an elongated sample from the specimen (page 53, paragraph spanning left to right column).

Regarding Claim 3, Enghardt et al disclose the method wherein the specimen is from a tumor (Fig. 3).

Regarding Claim 4, Enghardt et al disclose the method wherein the donor specimen is from a population of cells i.e. tumor tissue (Fig. 3).

Regarding Claim 5, Enghardt et al disclose the method wherein the donor specimen is from a cytological preparation i.e. tumor cells (Fig. 3).

Regarding Claim 6, Enghardt et al disclose the method wherein placing the donor specimen in an assigned location comprises forming an elongated receptacle in a donor block (page 52, right column), obtaining an elongated specimen (page 53, right column) and obtaining a plurality of copies by sectioning the array transverse to the donor specimen (page 53, right column, "slides" and Fig. 2).

Regarding Claim 7, Enghardt et al disclose the method wherein the donor specimen is placed in a receptacle having a size and shape "complementary" to the size and shape of the specimen (page 52, right column and page 53, right column).

Regarding Claim 8, Enghardt et al disclose the method wherein forming the elongated receptacle comprises forming a cylindrical bore in the recipient block and the donor specimen is obtained by boring a cylindrical tissue specimen from the donor block wherein the diameters of the receptacle and donor are substantially the same (pages 52-53).

Regarding Claim 9, Enghardt et al disclose the method further comprising associating a clinical characteristic with each assigned location i.e. diagnosis (page 55, first paragraph).

Regarding Claim 10, Enghardt et al disclose the method wherein a different analysis is performed on each array (page 54, left column and page 52, Table 1).

Regarding Claim 11, Enghardt et al disclose the method wherein the analysis is immunological analysis (page 54, left column and page 52, Table 1).

Regarding Claim 12, Enghardt et al disclose the method further comprising determining whether there are correlations between clinical characteristics associated with each location (page 55, left column).

Regarding Claim 13, Enghardt et al disclose the method wherein the sample is a tissue specimen (Fig. 3).

Regarding Claim 14, Enghardt et al disclose the method wherein clinical characteristics are determined apart from array analysis and the characteristics are tumor grade, size or status i.e. diagnosis (page 55, first paragraph).

Regarding Claim 15, Enghardt et al disclose the method wherein placing the specimen comprises placing a sample in a "corresponding" position of the multiple copies i.e. the samples are aligned relative to the sectioned arrays (page 55).

Regarding Claim 16, Enghardt et al disclose a method of parallel analysis of biological specimens comprising forming a donor block comprising a biological specimen embedded in

embedding medium (page 51, right column and page 53) obtaining a plurality of donor specimens cores (page 53), boring recipient cores from recipient embedding medium form an array of elongated receptacles (page 52, right column) placing each donor cores in the elongated receptacles at assigned locations (page 53) seconding the recipient embedding medium transverse to the elongated receptacles (page 53 "slides") performing different biological analysis on each cross-section and comparing the results to determine correlations (page 53, last paragraph-page 54, left column).

Regarding Claim 17, Enghardt et al disclose the method further comprising comparing the results to clinical information about the specimen (page 54, left column and Fig. 3).

Regarding Claim 18, Enghardt et al disclose the method wherein the specimen is from a tumor (Fig.3).

Regarding Claim 19, Enghardt et al disclose the method wherein the analysis is immunological analysis (page 54, left column and page 52, Table 1).

Regarding Claim 20, Enghardt et al disclose the method further comprising comparing the results to clinical information about the subject from whom the specimen was obtained (page 55, left column and Fig. 3).

Regarding Claim 22, Enghardt et al disclose the method wherein the donor core is substantially cylindrical and has a diameter of "about" 1mm(page 53).

Regarding Claim 29-30, Enghardt et al disclose the method wherein the comparing comprises determination of protein expression by immunological analysis (Table 1 and page 53-54).

Regarding Claims 43-44, Enghardt et al disclose the method wherein the analyzing evaluates a reagent for diagnosis i.e. antibody (Fig. 3).

Regarding Claim 49, Enghardt et al disclose the method wherein donor specimens are from one or more tumors (Fig.3).

Regarding Claim 53, Enghardt et al disclose a method of analyzing cellular specimens in a matrix with specimens positioned at predetermined known locations such that multiple copies of the matrix are provided in a two dimensional array, the method comprising exposing sequential copies of the matrix to an agent which interacts with the specimens to identify specimens which share a biological property i.e. antibody binding (pages 53-54).

Regarding Claim 54, Enghardt et al disclose the method wherein the specimens are provided in an elongated form and multiple copies are made by sectioning from a three dimensional array such that sequential section maintain a predetermined relationship (page 52, right column and page 53, right column).

Regarding Claim 55, Enghardt et al disclose the method wherein the shared biological property is a molecular characteristic i.e. antibody binding partner (Table 1 and pages 53-54).

Regarding Claim 56, Enghardt et al disclose the method wherein the shared biological property is presence of a protein (Table 1).

Regarding Claim 57, Enghardt et al disclose the method wherein the property is a specific reaction with an antibody specific for a specimen of interest (Table 1).

Regarding Claim 58, Enghardt et al disclose the method wherein the property is "correlated" with an other characteristic of the specimens (Table 1). As stated above, the claim is unclear because "other characteristic" is not defined or described. Additionally, the claim language "correlated" is very broad and interpreted thusly. As such, the protein expression and antibody binding are two characteristics analyzed by Enghardt that meet the limitations of the claim.

Regarding Claim 59, Enghardt et al disclose the method wherein the property includes clinical information about the subject i.e. diagnosis (page 55, left column).

Regarding Claim 60, Enghardt et al disclose the method wherein clinical information includes tumor grade, size or status i.e. diagnosis (page 55, first paragraph).

Regarding Claim 61, Enghardt et al disclose the method wherein the specimen is a tissue specimen (Fig.3).

Regarding Claim 64, Enghardt et al disclose the array of Claim 53 (Fig.1).

Regarding Claim 65, Enghardt et al disclose the array of Claim 54 (Fig.1).

Regarding Claim 70, Enghardt et al disclose the method wherein the specimens comprise animal cells i.e. tissue cells (Fig. 3).

Regarding Claim 87, Enghardt et al disclose the method wherein the method does not destroy the morphology of the specimen (page 51, right column).

Regarding Claim 88, Enghardt et al disclose a method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (cassette, and page 55, second full paragraph), obtaining a plurality of copies of the recipient array such that the copies maintain their assigned locations (page 53, right column "slides"), performing analysis of each copy and comparing the results of the analysis i.e. immunostained and analyzed (page 53, last paragraph-page 54, left column).

Regarding Claim 89, Enghardt et al disclose the method of Claim 1 further comprising correlating information concerning the specimen with the analysis wherein the information includes tumor grade, size or status i.e. diagnosis (page 55, first paragraph).

Regarding Claim 90, Enghardt et al disclose a method of parallel analysis of biological specimens comprising forming a donor block comprising a biological specimen embedded in embedding medium (page 51, right column and page 53) obtaining a plurality of donor specimens cores (page 53), boring recipient cores from recipient embedding medium form an array of elongated receptacles (page 52, right column) placing each donor cores in the elongated receptacles at assigned locations (page 53) seconding the recipient embedding medium transverse to the elongated receptacles (page 53 "slides") performing analysis on each

cross-section and determining frequency (i.e. plus or minus binding) of antibody binding (page 53, last paragraph-page 54, left column).

Regarding Claim 91, Enghardt et al disclose the method further comprising obtaining donor specimens from a predetermined morphologically defined region of a tumor (e.g. controls and lymph nodes (page 53, left column and Fig. 3).

Regarding Claim 92, Enghardt et al disclose the method further comprising obtaining donor specimens from a predetermined cell structure (e.g. controls and lymph nodes (page 53, left column and Fig. 3).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 21, 45-48, 93-94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Enghardt et al (Journal of Histotechnology, 1995, 18(1): 51-55)

Regarding Claims 21, 93 and 94, Enghardt et al disclose a method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (cassette, and page 55, second full

paragraph), obtaining a plurality of copies of the recipient array such that the copies maintain their assigned locations (page 53, right column "slides"), performing analysis of each copy and comparing the results of the analysis i.e. immunostained and analyzed (page 53, last paragraph-page 54, left column) and further comprising obtaining donor specimens from a predetermined morphologically defined region of a tumor (e.g. controls and lymph nodes (page 53, left column and Fig. 3) and further comprising obtaining donor specimens from a predetermined cell structure (e.g. controls and lymph nodes (page 53, left column and Fig. 3).

Enghardt et al teach the method wherein the tissue section and block are maintained in close proximity for easy association between them (page 55, left column) but they do not teach alignment of the section above the donor block for tissue identification. However, it would have been obvious to one of ordinary skill in the art, having both the donor block and tissue section in close proximity, to align the two, one above the other, for convenient identification.

Regarding Claim 45-48, Enghardt et al teach the method wherein analysis specifically includes reagent analysis, quality control and analysis of differentiation (page 55, left column). They do not teach the intended uses recited in Claims 45-48. However, one of ordinary skill in the art would have been motivated to apply the method of Enghardt et al for claimed uses based on tissue being examined and anticipated diagnosis.

10. Claims 24-29, 31, 50-52, 62-63, 68-69, 71-78 and 86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Enghardt et al (Journal of Histotechnology, 1995, 18(1): 51-55) in view of Stapleton et al (U.S. Patent No. 6,103,192, issued 15 August 2000).

Regarding Claims 24-29 and 31, Enghardt et al disclose a method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (cassette, and page 55, second full paragraph), obtaining a plurality of copies of the recipient array such that the copies maintain their assigned locations (page 53, right column "slides"), performing analysis of each copy and comparing the results of the analysis i.e. immunostained and analyzed (page 53, last paragraph-page 54, left column).

Enghardt et al do not teach using a nucleic acid array to identify a biomarker. However, nucleic acid array identification of biomarkers was well known in the art at the time the claimed invention was made as taught by Stapleton et al (Column 1, lines 20-40).

Stapleton et al teach a similar method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (matrix)and performing analysis of the specimens using a nucleic acid microarray (Column 1, lines 20-40) wherein the marker is selected by genetic analysis; wherein the marker is for gene expression and altered gene expression in for various tumor and diagnostic analysis (Column 6, lines 1-25; Column 16, lines 15-18; and Example 7). Stapleton et al further teach a motivation for using the microarray analysis i.e. minimizes the amount of specimen required for analysis and eliminates the need to extract nucleic acids from the sample (Column 5, lines 1-5 and 33-37).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the nucleic acid microarray analysis of Stapleton et al to the specimen analysis of Enghardt et al for the expected benefits of inexpensive, rapid and

sensitive diagnosis of clinically important tumors at the nucleic acid level as taught by Stapleton et al (Column 5, lines 1-48).

Regarding Claims 50-52 and 86, Enghardt et al teach the method wherein a plurality of different tumor tissues are analyzed but they do not specifically teach breast, bladder or prostate tumors, or from a plurality of tumors of the same type. However, Stapleton et al teach the similar method wherein the specimen is breast and/or from plurality of tumors of the same or different type and wherein the method is applicable to any tissue (Column 6 and Example 5). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the tumor specimens of Enghardt and Stapleton by analyzing different specimens of the same tissue e.g. breast, prostate or bladder for the obvious benefits of comparative analysis of normal and patient specimens as taught by Stapleton (Column 6, lines 15-25).

Regarding Claim 62-63, 68-69, 71-78, Stapleton et al teach their method wherein the cellular specimen is a cellular suspension that has been converted into a solid specimen (Column 9, line 61-Column 10, line 14) and wherein the suspension is from a body fluid e.g. malignancy from one or more cell lines and immobilized on a support (Column 11, line 27-Column 12, line 50). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the tissue cells of Enghardt et al with clinically important cell suspensions as taught by Stapleton et al for the obvious benefits of inexpensive, rapid and sensitive diagnosis of clinically important specimens at the nucleic acid level as taught by Stapleton et al (Column 5, lines 1-48). Stapleton further teach the method wherein normal tissues are compared to patient tissues (Column 6, lines 20-25) but they do not specifically teach the normal tissues are from a model organism or at different stages of tumor progression. However, it would have been further obvious to analyze tumors from a model organism and/or at different stages of progression for the obvious benefits of providing a stage-specific analysis and subsequently providing stage-specific treatment based on the analysis.

11. Claims 32-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stapleton et al (U.S. Patent No. 6,103,192, issued 15 August 2000) in view of An et al (U.S. Patent No. 5,882,864, issued 16 March 1999).

Regarding Claim 32, Stapleton et al disclose the method of analyzing genetic changes and gene expression in a tissue specimen the method comprising screening multiple genes with a nucleic acid array and screening multiple biological specimens in a specimen array (matrix) with a nucleic acid probe (primer) to detect genes which are abnormally expressed wherein the results of specimen screening is used to detect the array (Column 16, lines 9-28) but they do not teach the screening is used to select an array. However, An et al teach a similar method of tissue specimen analysis wherein the analysis provides disease-specific probes for diagnosis of tumors (Column 2, line 56-Column 3, lines 9). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the probe selection of An et al to the method of Stapleton et al to thereby select the arrayed probes from their screening step for the expected benefit of providing an array of disease-specific probes for diagnosis of tumors as taught by An et al (Column 2, line 56-Column 3, lines 9).

Regarding Claims 33-34, Stapleton et al disclose the method wherein the screening comprises high throughput genomic technique i.e. oligonucleotide arrays (Column 16, lines 9-36).

Regarding Claim 35, Stapleton et al teach the method wherein screening comprises searching database or other biomedical information sources as exemplified by their primer selection/design based on known sequences (Column 5, lines 61-63; Column 11, lines 30-37; and Example 1: Column 16, line 64-Column 17, line 22).

Regarding Claim 36, Stapleton et al teach the method wherein the screening comprises using a probe array (Column 16, lines 9-28) and they further teach their method detects mRNAs (Column 6, lines 11-25). While they do not specifically teach their probe arrays are

cDNA arrays, it would have been obvious to one of ordinary skill in the art that probe arrays for mRNA detection comprise cDNAs. Therefore, one of ordinary skill in the art would have been motivated to apply cDNA arrays to the method of Stapleton for the obvious benefit of analyzing mRNA populations as Stapleton et al desires (Column 6, lines 11-25).

Regarding Claim 37, Stapleton et al disclose the method wherein the screening comprises an array that is assayed for mutation (Column 16, lines 9-59).

Regarding Claim 38, Stapleton et al disclose the method wherein the array comprises loci that undergo differential expression in cancer (Example 7).

Regarding Claim 39, Stapleton et al disclose the method wherein the screening comprises hybridizing nucleic acids associated with a cell with the array and determining which loci indicate differential expression (Column 5, lines 33-48; Column 16, lines 9-59; and Example 7). An et al teach the similar method of probe screening (Fig. 1-15).

Regarding Claim 40, Stapleton et al disclose the method further comprising selecting a target that undergoes differential expression and using the probe to screen the specimens (Column 5, lines 33-48; Column 16, lines 9-59; and Example 7). An et al teach the similar method of probe selection (Claim 2).

Regarding Claim 41-42, Stapleton et al disclose the method wherein the specimen is a tumor specimen (Column 6, lines 1-25) and An et al teach the tumor specimen (Fig. 1-15).

12. Claims 66 and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Enghardt et al (Journal of Histotechnology, 1995, 18(1): 51-55) in view of Stapleton et al (U.S.

Patent No. 6,103,192, issued 15 August 2000) and An et al (U.S. Patent No. 5,882,864, issued 16 March 1999).

Regarding Claims 66 and 67, Enghardt et al disclose a method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (cassette, and page 55, second full paragraph), obtaining a plurality of copies of the recipient array such that the copies maintain their assigned locations (page 53, right column "slides"), performing analysis of each copy and comparing the results of the analysis i.e. immunostained and analyzed (page 53, last paragraph-page 54, left column).

Enghardt et al do not teach using a nucleic acid array to identify a biomarker. However, nucleic acid array identification of biomarkers was well known in the art at the time the claimed invention was made as taught by Stapleton et al (Column 1, lines 20-40).

Stapleton et al teach a similar method of parallel analysis of biological specimens comprising obtaining a plurality of donor specimens, placing each donor specimen in an assigned location in a recipient array (matrix)and performing analysis of the specimens using a nucleic acid microarray (Column 1, lines 20-40) wherein the marker is selected by genetic analysis; wherein the marker is for gene expression and altered gene expression in for various tumor and diagnostic analysis (Column 6, lines 1-25; Column 16, lines 15-18; and Example 7). Stapleton et al further teach a motivation for using the microarray analysis i.e. minimizes the amount of specimen required for analysis and eliminates the need to extract nucleic acids from the sample (Column 5, lines 1-5 and 33-37).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the nucleic acid microarray analysis of Stapleton et al to the specimen analysis of Enghardt et al for the expected benefits of inexpensive, rapid and sensitive diagnosis of clinically important tumors at the nucleic acid level as taught by Stapleton et al (Column 5, lines 1-48).

Enghardt et al and Stapleton do not teach their screening is used to select a probe for an array. However, An et al teach a similar method of tissue specimen analysis wherein the analysis provides disease-specific probes for diagnosis of tumors and specifically her-2 analysis (Column 2, line 56-Column 3, lines 9 and Claim 2). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the probe selection and her-2 analysis of An et al to the method of Enghardt et al and Stapleton et al to thereby select the arrayed probes from their screening step for the expected benefit of providing an array of disease-specific probes for diagnosis of tumors as taught by An et al (Column 2, line 56-Column 3, lines 9).

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit: 1634
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